REMARKS

Claims 1 to 4, and 6 to 16 are in the application. Claims 1, 6, 7, 9, 10 and 15 have been amended. No new matter is believed added.

Rejection under 35 USC § 102

Claims 1 to 4 are rejected to under 35 USC § 102(b) as being anticipated by Zirkle et al. (US Patent 2,800,478 ('478)). Applicant respectfully traverses this rejection.

In the prior office action the rejection was over a Zirkle et al., J. Med. Pharm. Chem. Publication from 1962. This rejection is now over a Zirkle et al. US patent, a different citation and prior art reference. See Office Action, Page 6, Point 5, line 2 and line 3). It appears that due to this change in references that the finality of the office action is clearly in error. Applicants expressly request that the finality of the office action be removed, and the request for a continuation application put in abeyance until needed with the fees refunded.

It further appears that the examiner is referring to a publication in the outstanding rejection, and not the US patent, although the image in the textual material of the Office Action is from a US patent. (See Office Action, page 7). These two references are not the same and this is an improper reference to one over the other. Clarification is requested.

The Examiner points out that a compound having Registry # 106655-97-4 is taught in what appears to be the image file extract of Col. 9 from US Patent 2,800,478 (See Office Action, page 7).

The Examiner then comments that "Clearly ethanol solutions of these compounds can be inhaled or taken orally. They were hydrogenated in ethanol, and also recrystallized form ethanol or ethanol/ether". This sentence is incomplete. It is not clear what the Examiners intent was. Clarification is requested.

The Examiner comments directed to ethanolic solutions are however, improper. There is no solely ethanolic solution shown in the '478 patent. It is an ethanol/ether recrystallization mixture. There is also no disclosure, nor suggestion, that such a mixture is suitable for inhalation in a mammal. The Examiner is taking an unsupported leap that this recrystallization mixture is a composition which could be used for inhalation treatment. More importantly though, there is no disclosure in these

references that inhalation was a route of administration contemplated by Zirkle at that time.

However, in order to advance prosecution, Applicants have amended the pharmaceutical composition claim, Claim 1, to recite that the composition be a dry powder inhalation composition comprising compounds of Formula (I).

Neither the Zirkle et al. J. Med Chem. article, nor US Patent 2,800,478 describe a dry powder pharmaceutical composition of the compounds of Formula (I) with excipients or carriers designed therein for inhalation therapy via the mouth. It should be noted that oral administration is accepted to mean swallowed and that absorption of the active agent is via the gastrointestinal tract. In contrast, inhalation therapy via the mouth or nose is directed to topical administration via the lung tissue.

Consequently, there can be no anticipation of the claims as amended, by either the Zirkle et al. publication or patent.

Therefore, in view of these remarks and amendments, reconsideration and withdrawal of the rejection to the claims under 35 USC §102 over Zirkle et al. is respectfully requested.

Rejection under 35 USC § 112

The rejection to Claims 6 to 15 is maintained under 35 USC § 112, first paragraph, as failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

The Examiner cites the In re Wands factors and specifically comments that the "claims are broad and drawn to many conditions, respiratory and otherwise but that's not really the main concern here, the main concern its that these compound have not been shown to be useful for treating any disease." (Office Action, page 8, Point (A)).

The Examiner has failed to properly read Claim 6. Claim 6 is merely recites a requirement that the composition (of Claim 1) inhibit the binding of acetylcholine to an acetylcholine receptor in a mammal. This method is not tied to the treatment of a particular disease state or respiratory condition as so noted by the Examiner. In fact, the specification provides more than ample support for such a claim. See the second binding assay, page 6, lines 16 to 24 which provides for a pan muscarinic antagonism screening against the M1 to M5 acetylcholine receptors. This is in fact a means to determine agonism or antagonism of each of the muscarinic receptors. The skilled

artisan would readily understand the significance of this assay and the potential limitations of compounds tested therein. This is a well known art recognized assay. The method of claim 6 does not require" treatment of a disease state". The claim limitations in Claim 6 are such that a compound of Formula (I) contact a particular receptor and that this contact is made by a route of administration, e.g. inhalation for receptors in the respiratory tract.

The first and the third described assay, appearing on pages 6, lines 26 to 31 through page 8, lines 1 to 15 are also variations on accepted *in vitro* assays.

More specifically and to address the Examiners point on page 8, the "Methacholine-induced bronchoconstrition –potency and duration of action" assay is clearly directed to *in vivo* usage in a mouse. This will also demonstrate inhibition of muscarinic acetylcholine receptors. Again, this is an accepted art recognized assay.

Applicants do not need to provide test data to show sufficiency of the specification. The art is now suitably predictable in this field that use of in vitro antagonism data will establish utility of the invention. As indicated the Examiners own comments, Zirkle et al. had in their possession the knowledge that compounds of Formula (I) where useful as anti-cholinergics. To have the Examiner now challenge that same information as used by Applicants is incomprehensible. Either Zirkle's utility is an acceptable utility or its not. Zirkle did not teach nor suggest the use of the compounds described therein for the treatment of disease states which require anticholinergic activity by route of administration which is inhalation therapy, suitably by the mouth with a dry powder inhalation composition. The instant specification does in fact provide to the skilled artisan four (4) assays directly related to supporting the method claims herein. Data is not needed, and the Examiner has provided no basis to challenge the finding that these compounds are not anticholinergics when the very reference over which he has asserted a §102 rejection is for the same utility, albeit by a different route of administration.

The cited prior art compound, ipratropium is approved for the same disease which are disclosed and claimed herein, treatment of COPD, asthma, etc. No compound presently on the market is solely directed to inhibition of a particular sub-type, such as the M3 receptor. All of the compounds which are on the market have some pan muscarinic receptor inhibition or perhaps agonism. While perhaps it is

desirable to have only a "selective" M3 receptor inhibition, it is clearly unnecessary for efficacy against these diseases, as ipratropium and tiotropium are approved products.

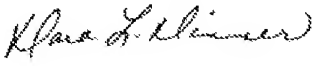
The specification provides for formulation details, amounts, how to use/administer such (dry powder formulations) of compounds of Formula (I), and reference additional patents on the various devices for such formulations.

In view of these remarks, reconsideration and withdrawal of the rejection to the claims is respectfully requested.

CONCLUSION

It is believed that the claims, as amended, are now all in condition for allowance. Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. It is not believed that this paper should cause any additional fees or charges to be required, other than expressly provided for already. However, if this is not the case, the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Respectfully submitted,



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